

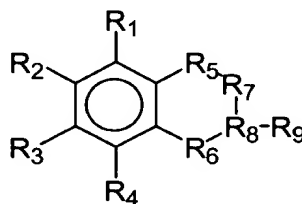
## In the Claims

Claims 1-6 (Cancelled)

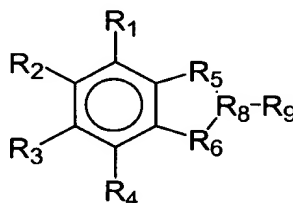
7. (Currently Amended) A ~~An angiogenesis inhibitory~~ composition comprising an angiogenesis inhibiting compound and an anti-inflammatory drug, wherein the angiogenesis inhibiting compound is ~~selected from~~:

(1) a compound of the formula

A)

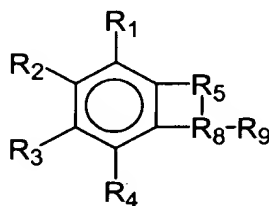


B)



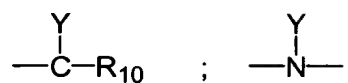
or

C)

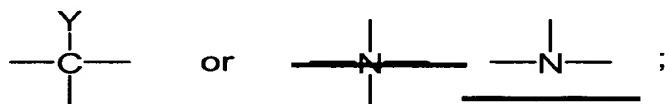


wherein R<sub>1</sub>-R<sub>4</sub> are each independently -H; -OH; =O; straight or branched chain alkanes, alkenes, or and alkynes; cyclic alkanes, alkenes, or and alkynes; a combinations of cyclic and acyclic alkanes, alkenes, or and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino, -XO<sub>n</sub> or -O-XO<sub>n</sub>, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; or

and halogens; R<sub>5</sub>-R<sub>7</sub> are each independently

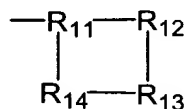


or -O-, where Y is absent and R<sub>10</sub> is =O<sub>2</sub> or Y and R<sub>10</sub> are each independently -H; -OH; =O; straight or branched chain alkanes, alkenes, or ~~and~~ alkynes; cyclic alkanes, alkenes, or ~~and~~ alkynes; a combinations of cyclic and acyclic alkanes, alkenes, or ~~and~~ alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino, -XO<sub>n</sub> or -O-XO<sub>n</sub>, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; or ~~and~~ halogens; ~~where~~ R<sub>8</sub> is:

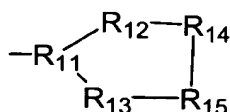


and R<sub>9</sub> is

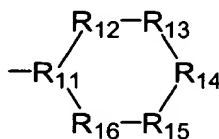
D)



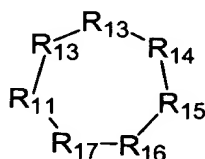
E)



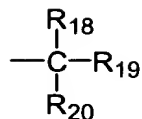
F)



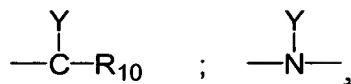
G)



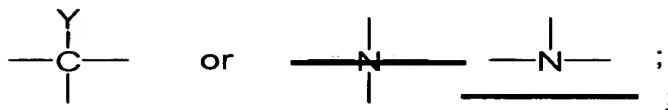
or H)



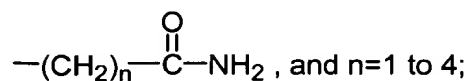
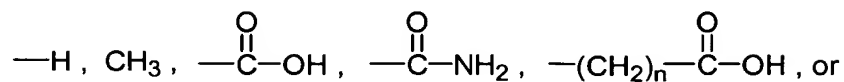
wherein each of  $R_{12}$ - $R_{17}$  is independently



wherein  $R_{11}$  is

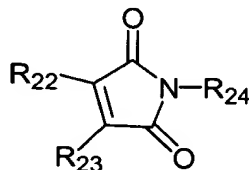


and wherein  $R_{18}$ ,  $R_{19}$  and  $R_{20}$  are each independently



with the proviso that the angiogenesis inhibiting compound is not thalidomide;

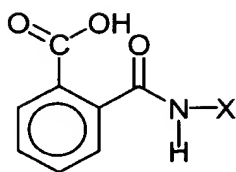
(2) a compound of the formula



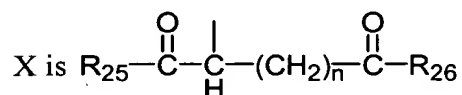
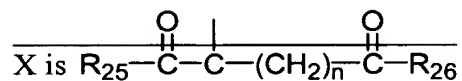
where  $R_{22}$  and  $R_{23}$  are each independently H, F, Cl, Br, I,  $CH_3$ , or  $-CH_2-CH_3$ ; and  $R_{24}$  is H,  $CH_3$ , or  $-CH_2-CH_3$ ;

or and

(3) a compound of the formula



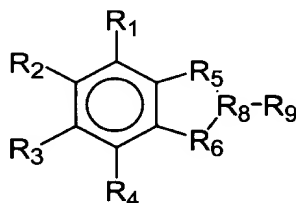
where X is R<sub>6</sub> as defined in (1) above, or



and R<sub>25</sub> and R<sub>26</sub> are independently -OH, -H, or -NH<sub>2</sub>, and n = 1 through 4.

8. (Previously Presented) The angiogenesis inhibitory composition of Claim 7 wherein the angiogenesis inhibiting compound is of the formula

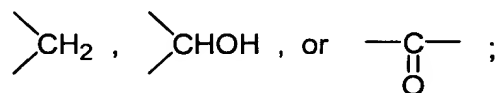
B)



and R<sub>5</sub> and R<sub>6</sub> are independently



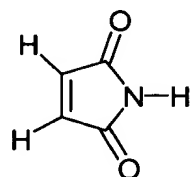
and R<sub>9</sub> is F) or H) wherein R<sub>14</sub> and R<sub>16</sub> are each independently



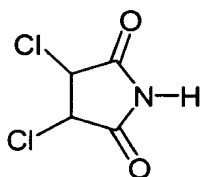
and R<sub>15</sub> is -O- or  $\text{>N}^{\text{R}_{21}}\text{>}$ , where R<sub>21</sub> is H, CH<sub>3</sub>, or OH.

9. (Currently Amended) The ~~angiogenesis inhibitory~~ composition of claim 7 wherein the angiogenesis inhibiting compound is

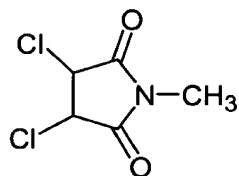
I)



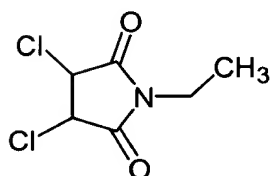
J)



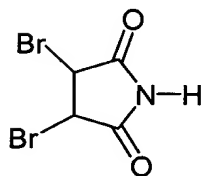
K)



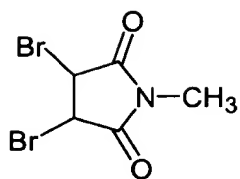
L)



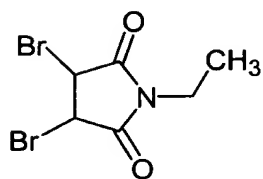
M)



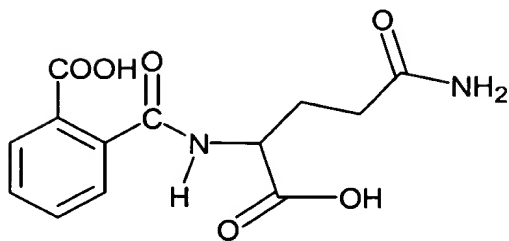
N)



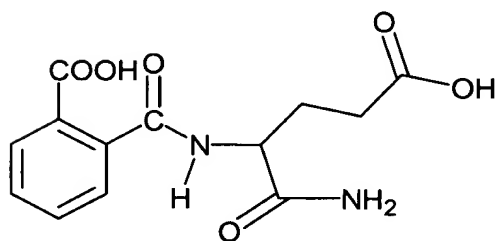
O)



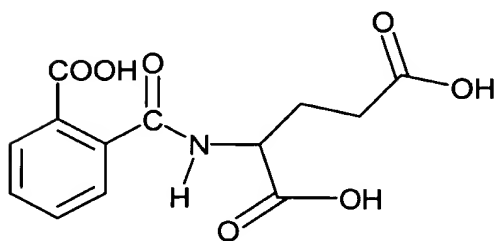
P)



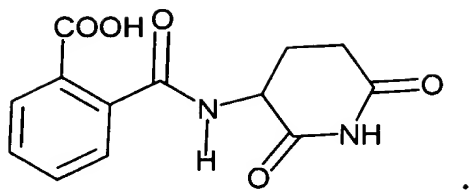
Q)



R)



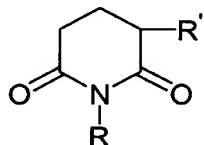
or S)



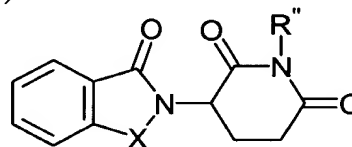
10. (Currently Amended) The ~~angiogenesis inhibitory~~ composition of Claim 7 wherein the angiogenesis inhibiting compound is a metabolites of thalidomide, thalidomide analogs, epoxides of thalidomide, hydrolysis products thereof, hydrolysis products of thalidomide, EM-12, metabolites of EM-12, epoxides of EM-12, hydrolysis products thereof, EM-138, metabolites of EM-138, epoxides of EM-138, hydrolysis products thereof, N-phthaloyl-DL-glutamic acid, N-phthaloyl-DL-glutamine anhydride, or mixture thereof.

11. (Currently Amended) The ~~angiogenesis inhibitory~~ composition of Claim 10 wherein the angiogenesis inhibiting compound is

(I)



(II)

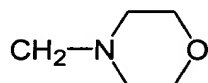


or

wherein

R is H, (C<sub>1</sub>-C<sub>6</sub>)alkyl, phenyl, or benzyl; and R' is phthalimido or succinimido;  
wherein

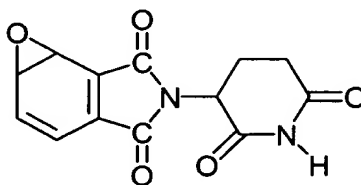
X is CH<sub>2</sub> or C=O; and R'' is H, -CH<sub>2</sub>CH<sub>3</sub>, -C<sub>6</sub>H<sub>5</sub>, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>, -CH<sub>2</sub>CH=CH<sub>2</sub>, or



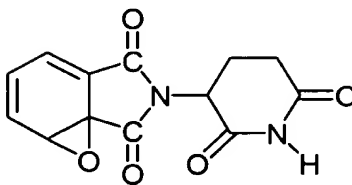
or (III) hydrolysis products of (II), wherein R'' is H and the piperidino ring or both the piperidino and the imido ring are hydrolyzed.

12. (Currently Amended) The ~~angiogenesis inhibitory~~ composition of Claim 10 wherein the angiogenesis inhibiting compound is

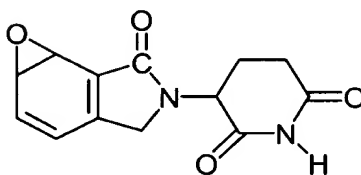
III)



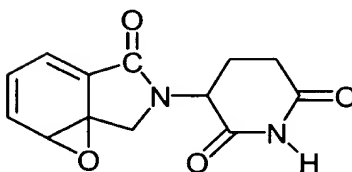
IV)



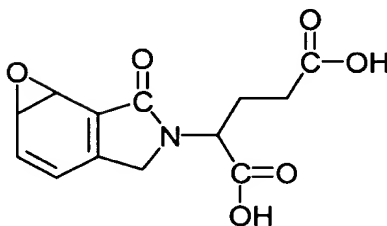
V)



VI)

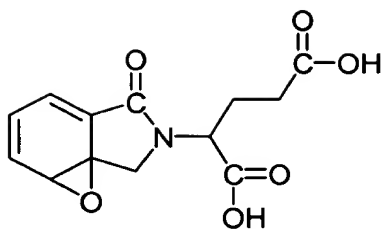


VII)

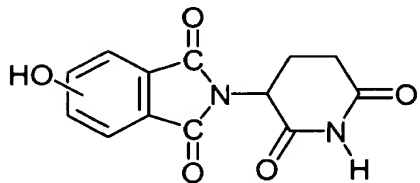




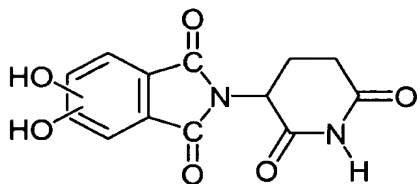
VIII)



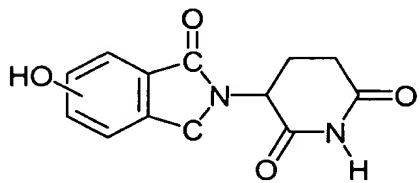
IX)



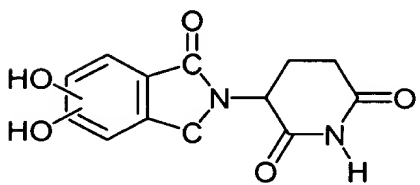
X)



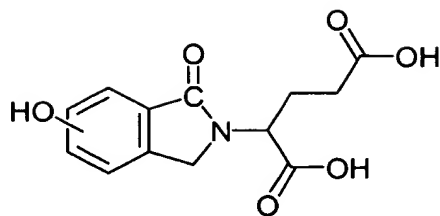
XI)



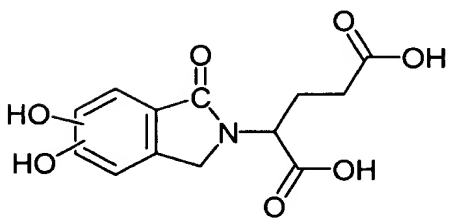
XII)



XIII)



or XIV)



Claims 13-14 (Cancelled).

15. (Previously Presented) A method for inhibiting angiogenesis in a human or animal comprising administering to the human or animal a composition comprising an angiogenesis inhibiting compound and an anti-inflammatory compound, with the proviso that the angiogenesis inhibiting compound is not thalidomide.

Claims 16-18 (Cancelled).

19. (Previously Presented) A method for treating an angiogenesis dependent disease in a human or animal having such a disease comprising administering to the human or animal in need of such treatment a composition comprising an angiogenesis inhibiting compound and an anti-inflammatory compound, with the proviso that the angiogenesis inhibiting compound is not thalidomide.

20. (Previously Presented) The method of Claim 19 wherein the angiogenesis dependent disease is macular degeneration, diabetic retinopathy, neovascular glaucoma, retrolental fibroplasia, proliferative vitreoretinopathy, solid tumors, blood-borne tumors, leukemia, hemangioma, psoriasis, Kaposi's sarcoma, Chrohn's disease, ulcerative colitis, cancer, retinopathy of prematurity, corneal graft rejection, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior

limbic keratitis, pterygium keratitis sicca, sjogren's syndrome, acne rosacea, phlyctenulosis, syphilis, *Mycobacteria* infections, lipid degeneration, chemical burns, bacterial ulcers, fungal ulcers, *Herpes simplex* infections, *Herpes zoster* infections, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, rheumatoid arthritis, systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Stevens-Johnson disease, radial keratotomy, corneal graft rejection, sickle cell anemia, pseudoxanthoma elasticum, pemphigoid, Paget's disease, veinocclusion, artery occlusion, cartoid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, systemic lupus erythematosus, Eales' disease, Behcet's disease, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, post-laser complications, or rubeosis.

21. (Currently Amended) The ~~angiogenesis-inhibitory~~ composition of Claim 7 wherein the antiinflammatory drug is a steroid.

22. (Currently Amended) The ~~angiogenesis-inhibitory~~ composition of Claim 21 wherein the steroid is cortisol, corticosterone, hydrocortisone, hydrocortisol, cortisone, prednisone, prednisolone, dexamethasone, beclomethasone, betamethasone, mometasone, mometasone furoate, budesonide, triamcinolone acetonide, or fluticasone.

23. (Currently Amended) The ~~An angiogenesis-inhibitory~~ composition of Claim 7 wherein the anti-inflammatory drug is a nonsteroidal, anti-inflammatory drug.

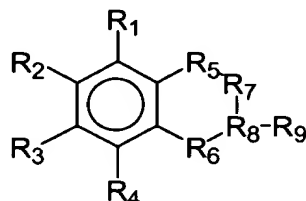
24. (Currently Amended) The ~~angiogenesis-inhibitory~~ composition of Claim 23 wherein the nonsteroidal, anti-inflammatory drug is aspirin, acetaminophen, ibuprofen, esculetin, phenidone, quercetin, ketoprofen, nordihydroguaiaretic acid, sulindac, sulindac sulfone, sulindac sulfide, indomethacin, NS-398, cyclooxygenase-1 inhibitors, methylheptyl imidazole, furegrelate sodium, SKF525AHCL, thromboxane inhibitors, toradol, ecase, salsalate, diflunisal, mefenamic acid, naproxen, naproxen sodium, flatafenine, meclofenamate, phenylbutazone, oxyphenbutazone, diclofenac, etodolac, fenoprofen, flufenamic acid, flurbiprofen, piroprofen, tolmetin, apazone, fenbufen, nabumetone, oxaprozin, piroxicam, salicylate, or tenoxicam.

25. (Currently Amended) The ~~angiogenesis-inhibitory~~ composition of Claim 23 wherein the nonsteroidal, anti-inflammatory drug is indomethacin or sulindac.

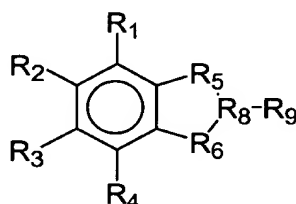
26. (Currently Amended) A method for inhibiting angiogenesis in a human or animal comprising administering to a human or animal in need of such inhibition a composition comprising an angiogenesis inhibiting compound and an anti-inflammatory compound, wherein the angiogenesis inhibiting compound is:

(1) a compound the formula

A)

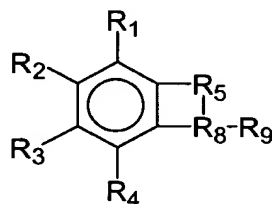


B)



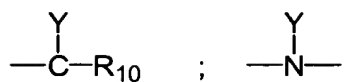
or

C)

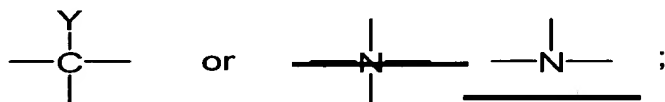


wherein

R<sub>1</sub>-R<sub>4</sub> are each independently -H; -OH; =O; straight or branched chain alkanes, alkenes, or ~~and~~ alkynes; cyclic alkanes, alkenes, or ~~and~~ alkynes; a combinations of cyclic and acyclic alkanes, alkenes, or ~~and~~ alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino, -XO<sub>n</sub> or -O-XO<sub>n</sub>, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; or ~~and~~ halogens; R<sub>5</sub>-R<sub>7</sub> are each independently

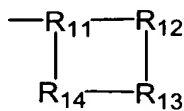


or -O-, where Y is absent and R<sub>10</sub> is =O or Y and R<sub>10</sub> are each independently -H; -OH; =O; straight or branched chain alkanes, alkenes, or ~~and~~ alkynes; cyclic alkanes, alkenes, or ~~and~~ alkynes; a combinations of cyclic and acyclic alkanes, alkenes, or ~~and~~ alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino, -XO<sub>n</sub> or -O-XO<sub>n</sub>, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; or ~~and~~ halogens; where R<sub>8</sub> is independently:

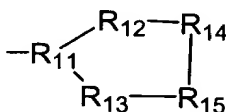


and R<sub>9</sub> is

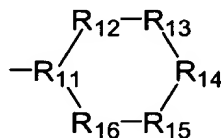
D)



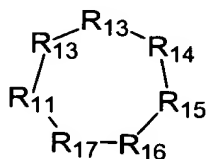
E)



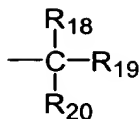
F)



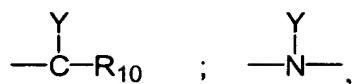
G)



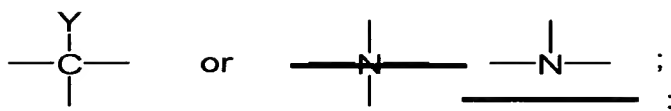
or H)



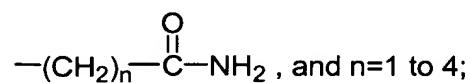
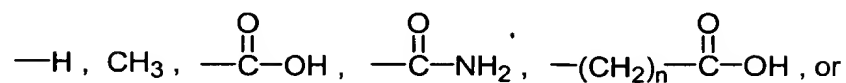
wherein each of  $R_{12}$ - $R_{17}$  is independently



wherein  $R_{11}$  is

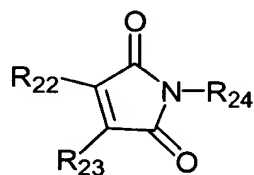


and wherein  $R_{18}$ ,  $R_{19}$  and  $R_{20}$  are each independently



with the proviso that the angiogenesis inhibiting compound is not thalidomide;

(2) a compound of the formula



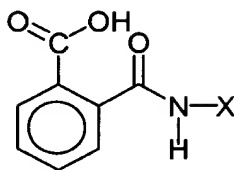
where  $R_{22}$  and  $R_{23}$  are each independently H, F, Cl, Br, I,  $CH_3$ , or

$-CH_2-CH_3$ ;

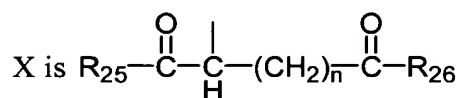
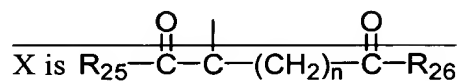
and  $R_{24}$  is H,  $CH_3$ , or  $-CH_2-CH_3$ ;

or and

(3) a compound of the formula



where X is R<sub>6</sub> as defined in (1) above, or

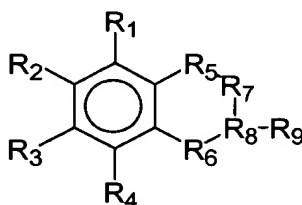


and R<sub>25</sub> and R<sub>26</sub> are independently -OH, -H, or -NH<sub>2</sub>, and n = 1 through 4.

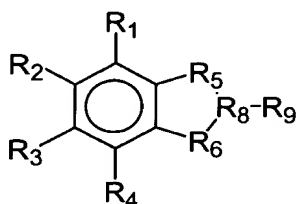
27. (Currently Amended) A method for treating an angiogenesis dependent disease in a human or animal having such a disease comprising administering to the human or animal in need of such treatment a composition comprising an angiogenesis inhibiting compound and an anti-inflammatory compound, wherein the angiogenesis inhibiting compound is:

(1) a compound of the formula

A)

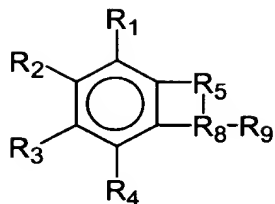


B)

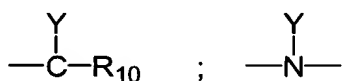


or

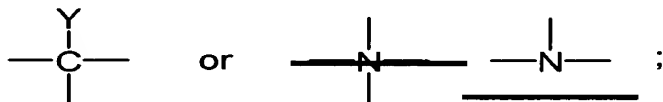
C)



wherein  $R_1$ - $R_4$  are each independently -H; -OH; =O; straight or branched chain alkanes, alkenes, or ~~and~~ alkynes; cyclic alkanes, alkenes, or ~~and~~ alkynes; a combinations of cyclic and acyclic alkanes, alkenes, or ~~and~~ alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino,  $-XO_n$  or  $-O-XO_n$ , where  $X=N$  and  $n=2$ ,  $X=S$  and  $n=2$  or  $3$ , or  $X=P$  and  $n=1-3$ ; or ~~and~~ halogens;  $R_5$ - $R_7$  are each independently

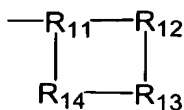


or -O-, where Y is absent and  $R_{10}$  is =O, or Y and  $R_{10}$  are each independently -H; -OH; =O; straight or branched chain alkanes, alkenes, or ~~and~~ alkynes; cyclic alkanes, alkenes, or ~~and~~ alkynes; a combinations of cyclic and acyclic alkanes, alkenes, or ~~and~~ alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino,  $-XO_n$  or  $-O-XO_n$ , where  $X=N$  and  $n=2$ ,  $X=S$  and  $n=2$  or  $3$ , or  $X=P$  and  $n=1-3$ ; or ~~and~~ halogens; where  $R_8$  is:



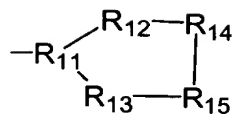
and  $R_9$  is

D)

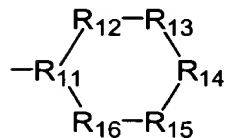




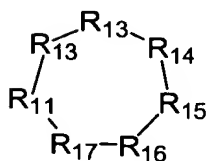
E)



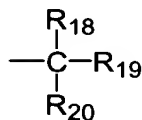
F)



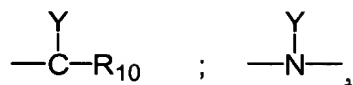
G)



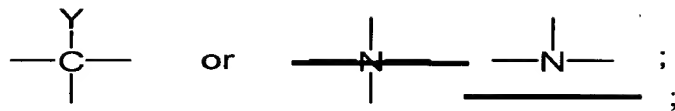
or H)



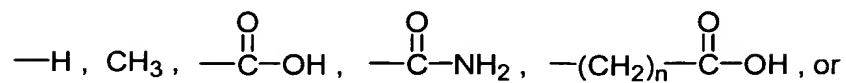
wherein each of  $R_{12}$ - $R_{17}$  is independently

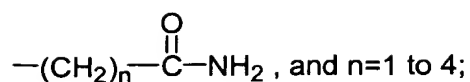


wherein  $R_{11}$  is



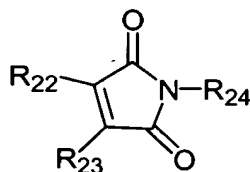
and wherein  $R_{18}$ ,  $R_{19}$  and  $R_{20}$  are each independently selected from





with the proviso that the angiogenesis inhibiting compound is not thalidomide;

(2) a compound of ~~selected from~~ the formula

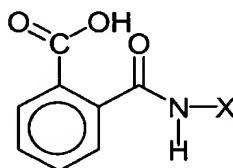


where  $R_{22}$  and  $R_{23}$  are each independently H, F, Cl, Br, I,  $\text{CH}_3$ , or  $-\text{CH}_2-\text{CH}_3$ ;

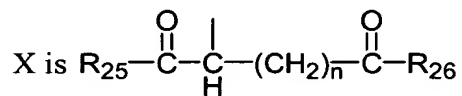
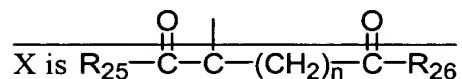
and  $R_{24}$  is H,  $\text{CH}_3$ , or  $-\text{CH}_2-\text{CH}_3$ ;

or and

(3) a compound of the formula



where X is  $R_6$  as defined in (1) above, or



and  $R_{25}$  and  $R_{26}$  are independently -OH, -H, or - $\text{NH}_2$ , and  $n = 1$  through 4.

28. (Previously Presented) The method of Claim 27 wherein the angiogenesis dependent disease is macular degeneration, diabetic retinopathy, neovascular glaucoma, retrolental fibroplasias, proliferative vitreoretinopathy, solid tumors, blood-borne

tumors, leukemia, hemangioma, psoriasis, Kaposi's sarcoma, Chron's disease, ulcerative colitis, cancer, retinopathy of prematurity, corneal graft rejection, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogren's syndrome, acne rosacea, phlyctenulosis, syphilis, *Mycobacteria* infections, lipid degeneration, chemical burns, bacterial ulcers, fungal ulcers, *Herpes simplex* infections, *Herpes zoster* infections, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, rheumatoid arthritis systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Stevens-Johnson disease, radial keratotomy, corneal graft rejection, sickle cell anemia, pseudoxanthoma elasticum, pemphigoid, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, systemic lupus erythematosus, Eales' disease, Behcet's disease, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, post-laser complications, or rubeosis.

Claims 29-31 (Cancelled).

32. (Previously Presented) The method of Claim 26 wherein the composition ~~comprises a formulation~~ is suitable for oral, rectal, ophthalmic, nasal, topical, vaginal, or parenteral administration.

33. (Previously Presented) The method of Claim 22 wherein the composition ~~comprises a formulation~~ is suitable for oral, rectal, ophthalmic, nasal, topical, vaginal, or parenteral administration.

34. (Previously Presented) The method of Claim 26 wherein the angiogenesis inhibiting compound is in a dosage of between about 0.1 mg/kg/day to about 300 mg/kg/day.

35. (Previously Presented) The method of Claim 34 wherein the dosage of the angiogenesis inhibiting compound is between about 0.5 mg/kg/day to about 50 mg/kg/day.

36. (Previously Presented) The method of Claim 35 wherein the dosage of the angiogenesis inhibiting compound is between about 1 mg/kg/day to about 10 mg/kg/day.

37. (Previously Added) The method of Claim 27 wherein the dosage of the angiogenesis inhibiting compound is between about 0.1 mg/kg/day to about 300 mg/kg/day.

38. (Previously Presented) The method of Claim 37 wherein the dosage of the angiogenesis inhibiting compound is between about 0.5 mg/kg/day to about 50 mg/kg/day.

39. (Previously Presented) The method of Claim 38 wherein the dosage of the angiogenesis inhibiting compound is between about 1 mg/kg/day to about 10 mg/kg/day.

Claims 40-42 (Cancelled)

43. (Previously Presented) An angiogenesis inhibitory composition of Claim 11 wherein the anti-inflammatory drug is a nonsteroidal, anti-inflammatory drug.

44. (Currently Amended) The ~~angiogenesis inhibitory~~ composition of Claim 43 wherein the nonsteroidal, anti-inflammatory drug is aspirin, acetaminophen, ibuprofen, esculetin, phenidone, quercetin, ketoprofen, nordihydroguaiaretic acid, sulindac, sulindac sulfone, sulindac sulfide, indomethacin, NS-398, cyclooxygenase-1 inhibitors, methylheptyl imidazole, furegrelate sodium, SKF525AHCL, thromboxane inhibitors, toradol, ecase, salsalate, diflunisal, mefenamic acid, naproxen, naproxen sodium, flocafenine, meclofenamate, phenylbutazone, oxyphenbutazone, diclofenac, etodolac, fenoprofen, flufenamic acid, flurbiprofen, piroprofen, tolmetin, apazone, fenbufen, nabumetone, oxaprozin, piroxicam, salicylate, or tenoxicam.

45. (Previously Presented) The method of Claim 15, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug.

46. (Previously Presented) The method of Claim 19, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug.

47. (Previously Presented) The method of Claim 26, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug.

48. (Previously Presented) The method of Claim 27, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug.